Advisory Action *Before the Filing of an Appeal Brief*	Application No.	Applicant(s)
	10/772,230	JOHANSSON, JAN
	Examiner	Art Unit	
	CHERIE M. WOODWARD	1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED <u>17 December 2007</u> FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

    a) ☒ The period for reply expires <u>6</u> months from the mailing date of the final rejection.

    b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

      Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

<u>NOTICE OF APPEAL</u>

2. ☒ The Notice of Appeal was filed on <u>*17 December 2007*</u>. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

<u>AMENDMENTS</u>

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will <u>not</u> be entered because

    (a)☐ They raise new issues that would require further consideration and/or search (see NOTE below);

    (b)☐ They raise the issue of new matter (see NOTE below);

    (c)☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

    (d)☒ They present additional claims without canceling a corresponding number of finally rejected claims.

      NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

    The status of the claim(s) is (or will be) as follows:

    Claim(s) allowed: _____.

    Claim(s) objected to: _____.

    Claim(s) rejected: <u>*5-9*</u>.

    Claim(s) withdrawn from consideration: _____.

<u>AFFIDAVIT OR OTHER EVIDENCE</u>

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will <u>not</u> be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will <u>not</u> be entered because the affidavit or other evidence failed to overcome <u>all</u> rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

<u>REQUEST FOR RECONSIDERATION/OTHER</u>

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Manjunath N. Rao, /
Supervisory Patent Examiner, Art Unit 1647

Continuation of 3. NOTE: Claims 1-4 were cancelled on 2/4/2004 in a preliminary amendment. Applicant has attempted to add new claims 10-13 without cancelling a corresponding number of finally rejected claims. Addtionally, Applicant has not amended claims 5-9 and the lack of amendments is not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal. In response to Applicant's arguments, Applicant states that they disagree with the rejection under 35 USC 102(b) as anticipated by Soto et al. Applicant argues that Soto et al., do not teach claim 5, which recites that the amino acid sequence of the protein be analyzed to determine whether they protein contains a predicted discordant helix. Applicant argues that predicting a discordant helix means "i.e. an amino acid sequence that is predicted to be able to form an alpha-helix and is also predicted to be able to form a beta-strand" (Remarks pp. 4, last paragraph, to page 5, first paragraph). Applicant also argues that Soto et al., only uses an algorithm to determine the probability of selected residues to form a beta-pleated sheet. Applicant argues that Soto et al., does not predict an alpha-helix. (Remarks, p. 5, first paragraph). Applicant argues that claim 5 requires the recognition that a sequence that can form an alpha-helix and a "beta-structure" is a particular type of sequence "a discordant sequence" and that such a structure has significance; "such a structure indicates that a protein containing the sequence can form amyloid" (Remarks, p. 5, first paragraph).

Applicant's argument has been fully considered, but it is not persuasive. Claim 5 reads on a method of identifying whether a protein is susceptible to forming amyloid comprising analyzing the amino acid sequence of the protein to determine whether the protein contains a predicted discordant helix, wherein the presence of the discordant helix is an indication that the protein is susceptible to forming amyloid. A "discordant helix" is defined in the specification at p. 4, lines 7-8 as "an amino acid sequence that is predicted to be able to form an alpha-helix and is also predicted to be able to form a beta-strand." The prior Office Action explicitly stated that Soto et al., use the Chou-Fasman structure prediction algorithm (see p. 3, second paragraph). The examiner also provided the Chou et al., reference, for exemplary purposes, as evidence of the way the Chou-Fasman algorithm works. The Chou-Fasman algorithm predicts sequences that can form alpha-helices or beta-sheets (see Chou et al., cited for exemplary purposes, throughout the document, but especially at pp. 257-259). Because Soto et al., explicitly states that they used the Chou-Fasman algorithm in their analysis and the Chou-Fasman structure prediction algorithm explicitly predicts "discordant helix" structure, as defined by applicant to mean "an amino acid sequence that is predicted to be able to form an alpha-helix and is also predicted to be able to form a beta-strand," Soto et al., meets all of the limitations of claim 5.

It is also noted that it is readily apparent that Applicant clearly understands what the Chou-Fasman analysis entails because Applicant attempts to claim a method using the Chou-Fasman analysis in new claim 12, which will not be entered.

Applicant argues against the examiner's analysis on page 3, last paragraph of the previous Office Action, that "Soto et al., teach that the hydrophobicity facilitates monomeric interactions that thermodynamically drive A-beta peptides to convert from alpha-helices to beta-sheets, which produce amyloid fibrils…Applicant's claims broadly encompass A-beta peptides, among others." (Remarks, p. 5, second paragraph). Applicant argues that in the referenced passage, Soto et al., refers only to beta-sheets and does not reference alpha-helical forms (Remarks, p. 5, second paragraph). Applicant also states that the examiner's statement that "Applicant's claims broadly encompass A-beta peptides among others" is unclear and requests clarification. Applicant argues that claim 5 is not drawn to a peptide (Remarks, p. 5, third paragraph). Applicant's arguments have been fully considered, but they are not persuasive. As discussed in detail above and in the Office Action of 6/15/2007, the Chou-Fasman algorithm used by Soto et al., explicitly teaches predictions of sequences in proteins that can form either alpha-helices or beta-sheets. In response to Applicant's confusion over the examiner's statement, claim 5 reads on a method of identifying whether a protein is susceptible to forming amyloid by the recited steps. As such, any protein, known or unknown, that is susceptible to forming amyloid, is encompassed within Applicant's method. The A-beta protein, taught by Soto et al., is protein that is well known to be susceptible to forming amyloid. As evidence in support of this fact, the examiner cited the Mihara et al., paper (see p. 3 of the previous Office Action, second paragraph). One of skill in the art would readily and immediately identify A-beta as a protein that could be used in the method of claim 5 such that a sequence analysis could be conducted in accordance with the steps of the claimed method in order to identify the presence of a predicted discordant helix. If Applicant needs additional clarification, they may contact the examiner for an interview.

Applicant also argues that approach taught by Soto et al., is not the same approach as taught by Applicant (Remarks, p. 6, first discussion paragraph). Applicant's argument has been fully considered, but is not persuasive. The method used by Soto et al., is the Chou-Fasman structure prediction algorithm, as discussed in detail above, that anticipates Applicant's claims, as discussed in detail in the previous Office Actions. Applicant argues that "[i]t appears that the Office Action is requiring a limit on the length of the discordant helices (Remarks, p. 6, last paragraph). Applicant's argument has been fully considered, but it is not persuasive. The examiner is not requiring a limit on the length of the discordant helices. Rather, the examiner is just pointing out the fact that the specification does not significantly limit the manner in which a discordant helix may be identified. It may be of any length (compare claim 5) or of at least six amino acids in length (compare claim 6). The exemplary limits set forth in the specification are exemplary limits only.

Applicant's Remarks on page 6, last full paragraph, state that "such methods are known in the art" when referring to the examiner's comment that the specification does not limit the manner in which "a discordant helix" may be identified. However, Applicant does not identify any reference where those methods are known. Because any references teaching the manner in which a discordant helix may be determined is materially relevant to the examination of the instant application, it is unclear whether Applicant is plainly admitting that the claimed method is already known in the art. If so, the examiner requests a full and complete disclosure of any and all art references known by Applicant or Applicant's representative that teach or disclose the manner in which a discordant helix may be identified (see Remarks, p. 6, last full paragraph).

With regard to claim 7, Applicant argues that nothing in Soto et al., relates to the identification of a discordant helix nor does Soto et al., suggest the stabilization of an alpha-helix form of a discordant helix (Remarks p.7, next to last paragraph). Applicant's argument has been fully considered, but it is not persuasive. The previous Office Action clearly states that Soto et al., teach that pH, peptide concentration, and solvents can influence the conformation of A-beta peptides and that these factors can determine whether the A-beta peptides adopt an alpha-helix or a beta-sheet conformation (Office Action p. 3, last paragraph, citing Soto et al., p. 673, first paragraph).

With regard to claims 8 and 9, Applicant argues that nothing in Soto et al., suggests making a compound that stabilizes an alpha-helical form of a discordant helix-containing polypeptide that forms amyloid   (Remarks, p. 7, last paragraph). Applicant also argues that because

Soto et al., does not anticipate claim 8, it cannot anticipate claim 9, which is dependent on claim 8. Applicant's arguments have been fully considered, but they are not persuasive. Page 4, first paragraph of the previous Office Action clearly states that Soto et al., teach the use of an inhibitor of A-beta fibrillogenesis peptide 1, called iA-beta-1, an 11 amino acid peptide that acts to stabilize and maintain alpha-helix conformation (see Soto et al., p. 674, second paragraph). Soto et al., also teach that other peptides and derivatives, including cyclic peptides or peptide mimetics may be used to prevent or retard amyloidosis in vivo in Alzheimer's disease and other types of amyloid related disorders (p. 678 to p. 679) (see previous Office Action at p. 4, second paragraph). Soto et al., teach each and every limitation of instant claims 5-9.

The after-final amendment will not be entered because the instant claims 5-9 have not been amended, they are not deemed to place the application in better condition for appeal by materially reducing or simplifying the issues for appeal. Additionally, the addition of four new claims without the corresponding cancellation of finally rejected claims is improper (see 37 CFR 1.116 and 41.33(a)).